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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,595	08/22/2003	Stanley W. Huth	14628/301681	9800

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ADVANCED MEDICAL OPTICS, INC.
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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,595	HUTH ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/22/03, 1/13/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 4-9 are pending in this application and were examined on their merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

The rejection of Claims 1 and 4-9 under 35 U.S.C. § 112, 1st paragraph, as failing to comply with the written description requirement has been withdrawn due to the Applicant's amendments to the claims filed 10/31/07.

The rejection of Claims 1, 4 and 6-8 under 35 U.S.C. § 102(b) as being anticipated by Kovács-Hadady *et al.* (1998) has been withdrawn due to the Applicant's amendments to the Claims filed 10/31/07.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 4-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cell-free system comprising the polymeric anti-microbial agent polyhexamethylene biguanide (PHMB) and the organic dye Eosin-Y, does not reasonably provide enablement for a cell free system comprising any polymeric antimicrobial agent and any organic dye, particularly any dye effective to dye Gram-positive organisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

There is no guidance or direction presented to direct one to determine which substances (antimicrobial agents) would work in the broadly claimed invention which is a complex and unpredictable art (i.e., an antimicrobial agent capable of binding to or complexing with the probe molecule/organic dye). Therefore because of the large number of inoperable embodiments claimed, the ordinary artisan would be subjected to undue experimentation to practice the claimed invention.

The entire scope of the claims has not been enabled because:

1. Quantity of experimentation necessary would be undue because of the large proportion of inoperative compounds claimed. The Applicants disclosure broadly lists several US patents

describing polymeric antimicrobials but no mention is made of whether or not any or these multiple diverse compounds are in fact capable of complexing with probe molecules consisting or organic dyes. Further, the disclosure lists several xanthene dyes such as Eosin-Y, S and B, Erythrosine B and fluorescein as preferred for staining gram-positive organisms, however it is known in the art that at least Eosin and erythrosine do not effectively stain either gram-positive or gram-negative cells alone needing a charge-transfer compound such as chlorpromazine See Molnár *et al.* (1992) Column 1, Lines 7-13).

2. Amount of direction or guidance presented is insufficient to predict which substances encompassed by the claims would work. One of ordinary skill in the art would be required to test each and every broadly described polymeric antimicrobial for the ability to complex with any random organic dye. Further, it is known in the art that other nonspecific compounds are capable of binding to or complexing with organic dyes such as Eosin-Y. For example, Waheed *et al.* (2000) teaches that Bovine serum albumin and other enzymes are capable of complexing with Eosin-Y and changing the absorbance spectrum of the solution (Pg. 130, Fig. 3). If other disparate compounds such as proteins and enzymes have the same complexing properties as the claimed polymeric antimicrobial compounds, one of ordinary skill in the art would have to test each and every polymeric antimicrobial to be ensured it would work as claimed. The disclosure does not mention any dyes effective to dye gram-positive organisms which also are able to complex with polymeric antimicrobial agents, a limitation particularly doubtful in view of the art which teaches that xanthene dyes alone are ineffective at staining bacteria.

3. Presence of working examples is only for specific substances and extension to other compounds has not been specifically taught or suggested. The Specification broadly claims and describes antimicrobials, of which some are polymeric, but does not address the necessary properties of complexing with organic dyes. The only demonstrated example is between the polymeric antimicrobial PHMB and the organic dye Eosin-Y, and extrapolation to any other polymeric antimicrobial/organic dye pair is neither taught nor specifically suggested.

4. The nature of the invention is complex and unpredictable. As discussed above, since organic dyes are capable of complexing with many diverse types of compounds beyond polymeric antimicrobials and therefore without specificity, unpredictability increases concomitantly.

5. The state of the prior art does not indicate that most related substances are not effective for the claimed functions. In fact, the prior art (cited patents) in the disclosure do not address the complexing properties of any polymeric antimicrobials and organic dyes are known to complex non-specifically as taught by Waheed *et al.* above. Further, Molnár *et al.* teaches that xanthine dyes are ineffective at staining gram-positive bacteria without a secondary charge-transfer compound, an effect not addressed in the disclosure.

6. Level of predictability of the art is very unpredictable. See above.

7. Breadth of the claims encompasses an innumerable number of compounds. Due to the large number of compounds claimed and the unpredictability inherent in the composition, the claims

encompass large numbers of polymeric antimicrobial compounds and any number of organic dyes.

8. The level of one of ordinary skill in this art is deemed to be high.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4 and 6-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Vehige *et al.* (2003).

Vehige *et al.* teaches a cell-free system for predicting the cellular activity of an agent comprising an Eosin-Y probe molecule, the agent PHMB, a test vessel for performing the assay that includes a multi-purpose buffer solution (water, pH 7.0) comprising PHMB and detect the complex formed by PHMB and Eosin-Y based on absorbance readings from a light spectroscope to detect the ionic complex formed by the polycationic PHMB and Eosin Y and graphing

calibration data correlating the spectral change with a reduction in *P. aeruginosa* microbes (Pg. 178, Column 1, Lines 1-14, Column 2, Lines 1-14 and Fig. 3 and Pg. 179, Fig. 6).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vehige *et al.* (2003) in view of Sawan *et al.* (WO 01/17357 A1).

The teachings of Vehige *et al.* were discussed above.

Vehige *et al.* dos not teach a method wherein the detector is a human eye.

Sawan *et al.* teaches the use of the polymeric antimicrobial compound Polyhexamethylene biguanide (PHMB) the organic dye Eosin-Y as a complexing agent to estimate the amount of PHMB visually (i.e., by the human eye) (Pg. 21, Lines 20-34 and Pg. 22, Table I).

It would have been one of ordinary skill in the art at the time of the invention to modify the cell-free system as taught by Vehige *et al.* by using the human eye as the means of detecting the interaction between Eosin-Y and PHMB because one of ordinary skill in the art would have recognized that certain organic dyes (Eosin-Y) are capable of being visually detected when reacting with a substrate, such as disclosed by Sawan *et al.* above. One of ordinary skill in the art would have been motivated to make this modification because the use of alternatives and functional equivalent techniques would have been desirable to those of ordinary skill in the art based upon the artisan's preference. One of ordinary skill in the art would have been motivated to use the human eye as a means of detecting the interaction of Eosin-Y with PHMB because the dye is known to be optically visible to the human eye. There would have been a reasonable expectation of success in making this modification because Eosin-Y is known in the art to be detected visually as well as spectrophotometrically.

Claims 1, 4 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovács-Hadady *et al.* (1998) in view of Sawan *et al.* (WO 01/17357 A1).

Kovács-Hadady *et al.* teaches a cell-free system for determining the presence of the preservative/antimicrobial Benzalkonium Chloride (BC), wherein the probe Eosin-Y (a dye molecule) is used to detect the presence of BC based on absorbance readings from a light spectroscope to detect the ionic complex formed by the cationic BC and Eosin Y (Pg. 735, Column 1, Lines 35-40 and Column 2, Lines 1-17 and Fig. 1).

Kovács-Hadady *et al.* teaches a test vessel for performing the assay that includes a multi-purpose buffer solution comprising BC (Pg. 735, Column 1, Lines 1-12)

It is inherent in the method of Kovács-Hadady *et al.* that the antimicrobial benzalkonium chloride is effective against at least one of *S. marcescens*, *S. aureus*, *P. aeruginosa*, *C. albicans* and *F. solani*, the light source for the spectrophotometer emits light radiation which inherently includes a band of wavelengths, and the detector measures the absorption resulting from the formation of a complex of the BC and Eosin Y. Data correlating the spectral change with a reduction in the number of live microbes when treated with the agent and a calibration graph including data are not parts of the system as claimed, constituting mental steps or calculations which do not materially change the system as claimed.

Although Kovács-Hadady did not explicitly teach a method for predicting the antimicrobial activity of an agent, the interaction between the BC and the Eosin is inherently

analogous to the interaction which would occur between the BC and a microbial cell membrane, since BC is known in the art to disrupt or destroy microbial cell membranes upon contact.

The MPEP states: The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Kovács-Hadady *et al.* does not teach wherein the antimicrobial agent is polymeric.

Sawan *et al.* teaches the use of the polymeric antimicrobial compound Polyhexamethylene biguanide (PHMB) the organic dye Eosin-Y as a complexing agent to estimate the amount of PHMB visually (i.e., by the human eye) (Pg. 21, Lines 20-34 and Pg. 22, Table I).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the cell-free system for determining the presence of the preservative/antimicrobial Benzalkonium Chloride (BC), wherein the probe Eosin-Y (an organic dye molecule) is used to detect the presence of BC based on absorbance readings from a light spectroscope to detect the ionic complex formed by the cationic BC and Eosin Y, as taught by Kovács-Hadady *et al.* above with the use of the polymeric antimicrobial compound PHMB as taught by Sawan *et al.* because one of ordinary skill in the art would have recognized PHMB as a

functional variation of BC, both being known in the art as having the utility of antimicrobial and complexing with Eosin-Y for purposes of determining the presence of the antimicrobial compound. One of ordinary skill in the art would have been motivated to make this modification because the use of alternatives and functional equivalent techniques would have been desirable to those of ordinary skill in the art based upon the economics and availability of compounds. There would have been a reasonable expectation in making this substitution because both compounds are known antimicrobials and known to complex with Eosin-Y.

Response to Arguments

Applicant's arguments filed 10/31/07 have been fully considered but they are not persuasive.

The Applicant argues that Kovács-Hadady *et al.* is directed to determining the presence of benzalkonium chloride in a solution and says nothing about prediction of antimicrobial or cellular activity (Remarks, Pg. 4, Lines 20-24),

In response to applicant's argument that Kovács-Hadady *et al.* says nothing about prediction of antimicrobial or cellular activity, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Applicant's arguments with respect to claims rejected in view of Park *et al.* have been considered but are moot in view of the new ground(s) of rejection above.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

12/28/07

/Jon P. Weber/
Jon P. Weber
Supervisory Patent Examiner, 1657